



Case Report

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Unusual Diagnosis and Extended Management of Chronic Inflammatory Demyelinating Polyneuropathy in an Unimmunized Patient

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Abstract

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a rare autoimmune disorder, often of idiopathic cause, but one that can result as a complication of Guillain Barre Syndrome (GBS). It often affects patients around 50-years of age, and impacts males twice as much as females. The treatment plan and management of the disease is still being investigated and developed. Our report describes findings consistent with CIDP in a pediatric patient, with an undiagnosed infectious prodrome. The goals of this case report are to increase knowledge to correctly diagnose these patients that may have an atypical presentation in the pediatric population and to add to the data for longitudinal management of the disease.

Background

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a rare autoimmune disorder, often of idiopathic cause but that can result as a complication of Guillain Barre Syndrome (GBS). It is characterized by hyporeflexia or areflexia with typically, descending weakness causing pure motor deficits (proximal and distal), although pure sensory or mixed deficits can also be seen. It often presents in middle-aged adults in their 50's with males affected twice as much as females. The incidence among adults is 1-2 cases per 100,000 people. However, CIDP incidence rate in patients under age 20 is 0.48 per 100,000 and the distal variant is more commonly encountered [1,2]. The diagnostic work-up and preferred treatment strategy for pediatric patients is similar to that of the adult population, as outlined by the European Federation of Neurological Societies/Peripheral Nerve Society Guideline in 2010 [3]. However, presentation of the disease in the pediatric population varies slightly from that of the adult population and pure motor symptoms are more often encountered. In this case, we aim to highlight this atypical presentation of CIDP and the further need for more recent guidelines to help with long term treatment for CIDP in pediatric patients.

Case

An 8-year-old unvaccinated female presented to Joe DiMaggio Emergency Department on November 2021 with chief complaints of stiffening of lower extremities, increased tendency to fall, and muscle weakness. The symptoms started one month prior to presentation and there was no

intercurrent illness or injury preceding onset of symptoms. Patient was otherwise healthy, had no known sick-contacts or COVID-19 exposure and her vaccine immunizations were not up to date. She continued with normal PO intake and urine output. She was afebrile on presentation and her physical exam was significant for abnormal gait with a pelvic tilt to the left side, absent patellar reflexes, and 1+ Achilles reflexes bilaterally, weakness of proximal lower extremity muscle groups, and scattered abrasions over the anterior shins and knees. Original laboratory workup in the Emergency Department (ED) included CK, troponin, CMP, CBC, urinalysis which were unremarkable. CT brain and lumbar X-rays were also obtained and found to be unremarkable.

The patient was admitted to the hospital for further workup and subsequent MRI imaging of the spine with and without contrast was significant for thickening and enhancement of the cauda equina, possibly suggestive of Guillain Barre Syndrome (GBS). Lumbar puncture was performed revealing cytoalbuminologic dissociation, as seen in Table 1, further

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Table 1: Cerebrospinal fluid cell analysis.

Spinal Fluid	December 2021 (Initial Admission)	February 2022 (Second Admission)	Normal Ranges
Glucose, CSF	56	54	40-70 mg/dL
Total protein, CSF	124 (H)	104 (H)	15-45 mg/dL
Appearance, CSF	Clear	Clear	
Color, CSF	Colorless	Colorless	
WBC Count, CSF	1	1	≤ 10 cells/mm ³
RBC Count, CSF	2	0	≤ 5 cells/mm ³
Macrophage, CSF	None seen	None seen	

suggestive of GBS. Given the history, clinical exam, CSF and MRI findings, the patient was diagnosed with GBS and treated with IVIG 2 G/kg administered as daily infusions over three days. The patient complained of hip pain and mild headaches during IVIG treatments, but symptoms subsided and clinically her gait was significantly improved after the third dose of IVIG. The patient was discharged six days after presentation with instructions to follow up with her primary pediatrician, the neurology team, and outpatient physical therapy.

Comparison of cerebrospinal fluid (CSF) cell count with differential results from the patient's initial and second hospital admission. Both CSF results show isolated elevation of total protein consistent with albumin cytological dissociation, which is reflective of widespread inflammation of nerve roots. This CSF finding is classically associated with Guillain-Barre Syndrome.

Less than three months after her initial hospitalization, the patient presented again in February 2022, for recurrence of symptoms over four days. She complained of gait instability, muscle weakness, and stuttering. The patient never followed up with the recommended outpatient providers due to the winter holiday season and it is unclear if her symptoms from initial presentation had completely resolved the day of presentation in February, the patient's muscle weakness and unsteadiness was significant enough that she was sent to the school nurse and her mother was contacted to pick her up from school. Her mother contacted the neurologist and was recommended to return to the ED. On presentation to the ED, the patient's physical exam was significant for weak hand grip, 4/5 strength in hips and ankles bilaterally, absent deep tendon reflexes bilaterally, altered gait with minimal hip flexion, modified Gower sign, and an inability to tiptoe, walk on her heels, or run with her arms extended. The working differential for her condition was expanded to include CIDP and the necessary studies were done to evaluate the diagnosis as per the European Joint task force diagnosis guidelines [3]. A repeat of the brain and spine imaging was not significant and a repeat lumbar puncture, as seen in Table 1, again found elevated protein. A cytokine panel was obtained which showed elevated NK cells, indicative of a possible viral etiology for her symptoms. Electromyogram and nerve conduction studies were conducted, as shown in Figure 1, consistent with motor and sensory demyelinating polyneuropathy. The clinical picture of the patient, as well as the lumbar puncture and EMG studies served to diagnose the child with CIDP. Throughout her hospital admission, the

patient's vitals were within normal limits, and she remained afebrile with adequate oral intake and urine output.

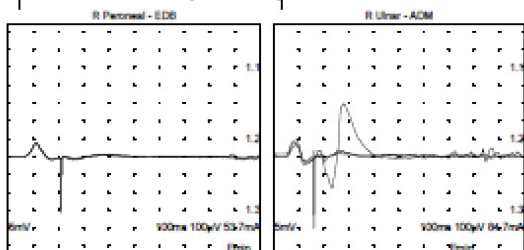
She was started on an IVIG regimen, as described in Łukawska, et al. 2021. The study indicated significant symptom remission with an initial IVIG dose of 2 g/kg over 5 days followed by a maintenance dose of 0.4-1.2 g/kg every 2-6 weeks along with a steroid treatment [4]. The patient was discharged from the hospital five days later, after the initial IVIG dose was completed, in February 2022. She had remarkable improvement of her leg strength and gait but was not symptom free. The patient's mother shared her personal concerns with frequent steroid use in the patient due to its side effects, so the decision was made to schedule her for monthly IVIG infusions only. She was scheduled for follow-up with the outpatient physical therapy rehabilitation clinic, the pediatric allergy and immunology clinic, and the pediatric neurology clinic as well as with her primary pediatrician.

Electrodiagnostic study showing generalized abnormalities consistent with motor and sensory demyelinating polyneuropathy. This pattern of electrodiagnostic along with the patient's prolonged clinical history is consistent with CIDP.

Findings:

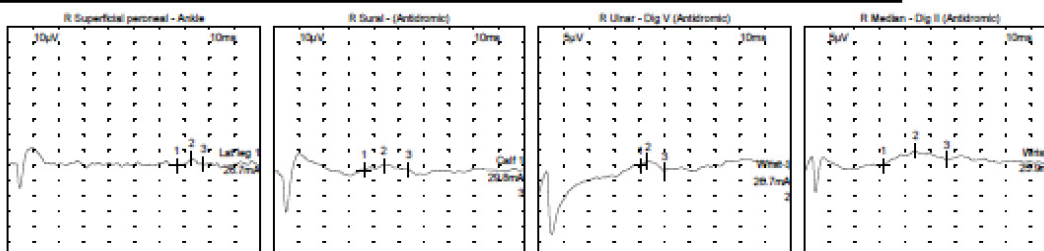
1. The right ulnar motor nerve shows normal digital latency and CMAP amplitude, however, there is evidence of conduction block below and across the elbow with significant decrease in the CMAP amplitudes and conduction velocities at these two sites. The F-wave for the ulnar nerve was also more than double of the expected latency.
2. The right peroneal motor nerve shows prolonged distal latency with normal CMAP amplitude with evidence of conduction block while stimulating below the fibular head with decreased CMAP amplitude and decreased conduction velocity. The F-wave for this nerve also showed a significant delay in the latency of more than double the expected value.
3. The right median sensory nerve shows prolonged latency and decreased conduction velocity with normal SNAP amplitude.
4. The right ulnar sensory nerves show prolonged latency with decreased conduction velocity and decreased SNAP amplitude.
5. The right sural sensory nerves show prolonged latency

Nerve	F min ms
R Ulnar - ADM	70.0



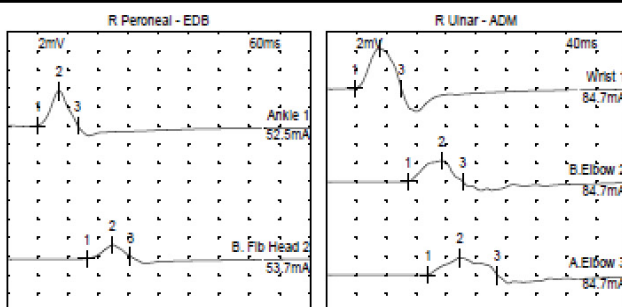
Sensory NCS

Nerve / Sites	Rec. Site	Onset Lat ms	Peak Lat ms	Amp µV	Segments	Distance mm	Velocity m/s	Temp. °C
R Median - Dig II (Antidromic)								
Wrist	Index	3.1	4.4	4.7	Wrist - Index	100	32	34
R Ulnar - Dig V (Antidromic)								
Wrist	Dig V	4.0	4.3	1.4	Wrist - Dig V	100	25	33.4
R Sural - (Antidromic)								
Calf	Ankle	3.6	4.4	3.0	Calf - Ankle	100	28	32.2
R Superficial peroneal - Ankle								
Lat leg	Ankle	6.7	7.3	4.2	Lat leg - Ankle	100	15	32.1



Motor NCS

Nerve / Sites	Muscle	Latency ms	Amplitude mV	Segments	Distance mm	Lat Diff ms	Velocity m/s	Temp. °C
R Ulnar - ADM								
Wrist	ADM	3.8	4.3	Wrist - ADM	60			34.7
B.Elbow	ADM	10.9	2.2	B.Elbow - Wrist	120	7.1	17	34.7
A.Elbow	ADM	13.5	1.8	A.Elbow - B.Elbow	80	2.6	30	34.7
R Peroneal - EDB								
Ankle	EDB	5.9	3.7	Ankle - EDB	60			33
B. Fib Head	EDB	15.6	1.5	B. Fib Head - Ankle	225	9.7	23	33.1



F Wave

Nerve	F min ms
R Peroneal - EDB	86.5

Figure 1: Abnormal electrodiagnostic study with resultant findings.

with decreased conduction velocity and normal SNAP amplitude.

6. The right superficial peroneal nerves show significant delay of the latency with decreased conduction velocity and normal SNAP amplitude.

On follow-up, the patient's monthly IVIG has been modified to an increased frequency of every three weeks due to a decreasing interval between her relapses. In accordance with her mother's preferences, she has never received steroid doses. She also is being followed by occupational and physical therapy to help her recover strength and resume daily activity level. Monthly laboratory findings consistently show normal immunoglobulin levels, but an elevation in her basophils and eosinophils, as well as an elevation in her total protein (8 g/dL), AST levels (55-60 g/dL) and a decreased alkaline phosphatase (< 160 g/dL). To prevent injuries and allow for more consistent adherence to her treatment plan, she has been placed in a homeschooling program temporarily for one semester.

Discussion

The incidence of Chronic inflammatory demyelinating polyneuropathy is 1-2 per 1,00,000 in adults, and 0.23-0.48 per 1,00,000 in children [1,2]. The rarity of this disease coupled with the lack of definitive evidence on treatment strategies makes the disease complex to diagnose and treat. This case highlights the atypical presentation of CIDP in the pediatric population and the challenges of its treatment, requiring monthly, if not weekly, management and multiple modalities of treatment. We present an unvaccinated pediatric patient, who develops CIDP most likely following a viral infection months earlier. The patient had originally presented and been diagnosed with Guillain-Barre Syndrome, an acute form of demyelinating polyneuropathy, month after the viral infection, and while 95% of patients usually recover with varying degree of remission, some, like our patient, go on to develop the chronic form of the disease [5].

The diagnosis of CIDP as outlined by the European Federation of Neurological Societies/Peripheral Nerve Society Guideline in 2010 [3], involves a clinical picture consistent with the presentation of progressive and relapsing muscle weakness, either symmetric or asymmetric, developing over eight weeks and with absent or decreased deep tendon reflexes. Their guidelines also emphasize confirming the diagnosis with electrodiagnostic criteria (EMG), showing at least two motor nerve abnormalities. Other supportive criteria include a CSF analysis showing cytoalbuminologic dissociation, nerve biopsy or response to treatment.

The widely preferred treatment for CIDP has been IVIG 1-2 mg/kg daily or on alternate days [1]. It has been suggested to add steroids into CIDP regiment, however, studies have found that it was not as beneficial in pure motor CIDP [3,6]. Long-term treatment with steroids is also usually used with caution because of the adverse effect on a pediatric patient's growth and bone development. Another treatment option, as recommended by the European Joint Task force guidelines [6], includes the use of plasmapheresis

in the case that IVIG and steroid treatment prove ineffective. Furthermore, they recommend adding immunosuppressants or immunomodulators if the maintenance dose is inadequate. The prognosis of CIDP in pediatric populations is generally good, with a remission rate of 51.4% and follow up period ranging from 10-222 months [4]. In our patient's case, steroids were avoided as maintenance therapy, and plasmapheresis was not started as an option since patient was responding to IVIG every 3 weeks. While the end-goal of her treatment is resolution of her symptoms, it is unclear at this time how aggressive the future treatment course will need to be and how long this presentation of CIDP will take to resolve.

In conclusion, more longitudinal studies will be useful in helping with consistent standard treatment strategies for pediatric CIDP.

Declaration

Ethics approval and consent to participate

This article does not contain any studies with human or animal subjects performed by any of the authors.

Consent for publication

Consent has been obtained from the legal guardian/parent.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due HIPAA, but are available from the corresponding author on reasonable request.

Competing interests

The authors of this manuscript declare no conflict of interest.

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Authors contributions

Danan V: Active participant in the care of the patient, primary author of the manuscript; Fridman S: Author and editor of the manuscript; Lopez C: Active participant in the care of the patient, author and editor of the manuscript; Basit A: Primary physician of the patient, author and editor of the manuscript.

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